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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/727,349 11/30/00 ENGELHARDT

D ENZ-52 (D1)

EXAMINER

HM12/0228

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CHAKRABARTI, A

ART UNIT

PAPER NUMBER

1655

DATE MAILED:

02/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/727,349

Applicant(s)

Engelhardt

Examiner

Arun Chakrabarti

Group Art Unit

1655



☒ Responsive to communication(s) filed on Feb 8, 2001

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-51 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-51 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Election/Restriction

1. Applicant has elected Group I corresponding to claims 1-51 with traverse. Applicant's election with traverse of Group I in Paper No. 3 is acknowledged. The traversal is on the ground(s) that reconsideration of the restriction requirement as to the claims of Groups I and III is requested. This is not found persuasive because applicant argues that there would be no burden in searching Group III with Group I. However, as the restriction makes clear, additional search of Group III would require review of class 435, subclass 91.1. Review of these additional searches is prima facie evidence of burden which is not rebutted.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected over the recitation of the phrase, "introduction of intermediate structure". It is not clear if the structure present in the nucleic acid to be produced is claimed or a helper molecule for the production of nucleic acid is claimed or a molecular structure in between

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the above mentioned molecules are claimed. It is not clear what are the phases between which the claimed intermediate structure belongs. The metes and bounds of the claim is vague and indefinite.

Claim Rejections - 35 U.S.C. § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-6, 8-9, 14-15, 18-21, 26 and 28-29 are rejected under 35 U.S.C. 102 (b) as being anticipated by Kacian et al. (U.S. Patent 5,399,491) (March 21, 1995).

Kacian et al teach an in vitro process for producing more than one copy of a specific nucleic acid, the process being independent of a requirement for the introduction of an intermediate structure for the production of the specific nucleic acid (Abstract and Figure 1J and Column 17, lines 34-38), the process comprising the steps of :

a) providing a nucleic acid sample containing or suspected of containing the sequence of the specific nucleic acid (Abstract, Figure 1J and Column 17, lines 34-38);

b) contacting the sample with a mixture comprising :

(I) nucleic acid precursors (Figure 1J and Column 17, lines 34-38),

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(ii) one or more specific nucleic acid primers each of which is complementary to a distinct sequence of the specific nucleic acid (Figure 1J and Column 17, lines 34-38), and

(iii) an effective amount of a nucleic acid producing catalyst (Figure 1J and Column 17, lines 34-38); and

c) allowing the mixture to react under isostatic conditions of temperature, buffer and ionic strength, thereby producing more than one copy of the specific nucleic acid (Figure 1J and Column 17, lines 34-38 and Abstract).

Kacian et al teach an in vitro process wherein the specific nucleic acid is single-stranded (Figure 1J and Column 17, lines 34-38).

Kacian et al teach an in vitro process wherein the specific nucleic acid is ribonucleic acid.(Figure 1J).

Kacian et al teach an in vitro process wherein the specific nucleic acid is in solution (Column 25, lines 44-60).

Kacian et al teach an in vitro process further comprising the step of treating the specific nucleic acid with a blunt-end promoting restriction enzyme (Figure 1J).

Kacian et al teach an in vitro process wherein the specific nucleic acid is isolated prior to the contacting step (b) (Figure 1J).

Kacian et al teach an in vitro process wherein the captured nucleic acid is carried out by restriction enzyme (Figure 1J).

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Kacian et al teach an in vitro process wherein the specific nucleic acid primers is deoxyribonucleic acid (Figure 1J).

Kacian et al teach an in vitro process wherein the specific nucleic acid primers contain no more than five complementary base pairs and comprise from about 5 to 100 nucleotides (Column 24, lines 52-63).

Kacian et al teach an in vitro process wherein the nucleic acid producing catalyst is selected from DNA polymerase and reverse transcriptase (Figure 1J).

Kacian et al teach an in vitro process further comprising the step (d) of detecting the product produced in step c) (Figures 6a and 6b).

Kacian et al teach an in vitro process wherein the detecting step is carried out by means of incorporating into the product a labeled primer (Figures 6a and 6b).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-9, 14-15, 18-21, 26 and 28-29 are rejected under 35 U.S.C. 103 (a) over Kacian et al. (U.S. Patent 5,399,491) (March 21, 1995) in view of Bernstein et al. (U.S. Patent 6,183,961 B1) (February 6, 2001).

Kacian et al teach the method of claims 1-6, 8-9, 14-15, 18-21, 26 and 28-29 as described above.

Kacian et al do not teach the process wherein the isolation of specific nucleic acid is carried out by means of sandwich capture.

Bernstein et al. teach the process wherein the isolation of specific nucleic acid is carried out by means of sandwich capture. (Column 16, lines 52-56).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the sandwich capture of Bernstein et al. into the method of Kacian et al ., since Bernstein et al. state, "For example, sandwich assays are commercially useful hybridization assays for detecting or isolating nucleic acid sequences (Column 16, lines 52-54)." An ordinary practitioner would have been motivated to combine and substitute the sandwich capture of Bernstein et al. into the method of Kacian et al ., in order

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to achieve the express advantages , as noted by Bernstein et al., of an assay which is commercially useful hybridization assay for detecting or isolating nucleic acid sequences.

8. Claims 1-6, 8-9, 14-15, 18-21, 26 , 28-35, and 39-42 are rejected under 35 U.S.C. 103 (a) over Kacian et al. (U.S. Patent 5,399,491) (March 21, 1995) in view of Jones (U.S. Patent 6,190,889 B1) (February 20, 2001).

Kacian et al teach an in vitro process of claims 1-6, 8-9, 14-15, 18-21, 26 and 28-29 as described above including the enzyme ribonuclease H.

Kacian et al do not teach an in vitro process for producing more than one copy of a specific nucleic acid, the products being substantially free of any primer-coded sequences by using chemically modified primers and removing substantially or all primer-coded sequences from the product produced in step to regenerate a primer binding site, thereby allowing a new priming event to occur and producing more than one copy of the specific nucleic acid.

Jones teaches an in vitro process for producing more than one copy of a specific nucleic acid, the products being substantially free of any primer-coded sequences using chemically modified deoxyribonucleic acid primers and removing substantially or all primer-coded sequences from the product produced in step to regenerate a primer binding site, thereby allowing a new priming event to occur and producing more than one copy of the specific nucleic acid (Abstract and Claim 1).

Kacian et al do not teach an in vitro process wherein the removing is carried by digestion with an enzyme.

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Jones teaches an in vitro process wherein the removing is carried by digestion with an enzyme.(Claims 1 and 2).

Kacian et al do not teach an in vitro process wherein a primer binding site is regenerated, thereby allowing a new priming event to occur and producing more than one copy of the specific nucleic acid.

Jones teaches an in vitro process wherein a primer binding site is regenerated, thereby allowing a new priming event to occur and producing more than one copy of the specific nucleic acid. (Column 42, line 46 to column 43, line 31).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method for removing primer sequences of Jones into the method of Kacian et al., since Jones states, "Thus, the invention pertains to novel methods for generating staggered templates and for iterative and regenerative DNA sequencing as well as to methods for automated DNA sequencing (Column 4, lines 37-40)." An ordinary practitioner would have been motivated to combine and substitute the method for removing primer sequences of Jones into the method of Kacian et al.. in order to achieve the express advantages , as noted by Jones., of an invention that pertains to novel methods for generating staggered templates and for iterative and regenerative DNA sequencing as well as to methods for automated DNA sequencing .

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9. Claims 1-6 and 8-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kacian et al. (U.S. Patent 5,399,491) (March 21, 1995) in view of Jones (U.S. Patent 6,190,889 B1) (February 20, 2001) further in view of Ward et al. (U.S. Patent 4,711,955) (December 8, 1987).

Kacian et al in view of Jones teach the in vitro process of claims 1-6, 8-9, 14-15, 18-21, 26, 28-35, and 39-42 as described above.

Kacian et al in view of Jones do not teach the process wherein at least one modified nucleotide or nucleotide analog selected from cytidine 5'-triphosphate or deoxy cytidine 5'-triphosphate.

Ward et al teach the process wherein at least one modified nucleotide or nucleotide analog selected from cytidine 5'-triphosphate or deoxy cytidine 5'-triphosphate (Column 3, lines 20-39 and Examples 3 and 4).

Kacian et al in view of Jones do not teach the process wherein the analog is modified on the sugar.

Ward et al teach the process wherein the analog is modified on the sugar (Abstract and Column 3, lines 20-39).

Kacian et al in view of Jones do not teach the process wherein the analogs comprise from about 1 to about 200 nucleotide.

Ward et al. teaches the process wherein the analogs comprise from about 1 to about 200 nucleotide. (Column 5, line 1 to Column 6, line 32).

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Kacian et al in view of Jones do not teach the process wherein the base sequences are linked together by other than a phosphodiester bond.

Ward et al. teaches the process wherein the base sequences are linked together by other than a phosphodiester bond. (Claim 8).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the modified nucleotide or nucleotide analog of Ward et al. into the nucleic acid sequence amplification method of Kacian et al in view of Jones, since Ward et al. state, "The interaction between modified nucleotides and specific proteins can be utilized as an alternative to radioisotopes for the detection and localization of nucleic acid components in many of the procedures currently used in biomedical and recombinant-DNA technologies. Methods employing these modified nucleotide-protein interactions have detection capacities equal to or greater than procedures which utilize radioisotopes and they often can be performed more rapidly and with greater resolving power. These new nucleotide derivatives can be prepared relatively inexpensively by chemical procedures which have been developed and standardized as discussed more fully hereinafter. More significantly, since neither the nucleotide probes of this invention nor the protein reagents employed with them are radioactive, the compounds can be prepared, utilized and disposed of without the elaborate safety procedures required for radioisotopic protocols. Moreover, these nucleotide derivatives are chemically stable and can be expected to have functional shelf-lives of several years or more. Finally, these compounds permit the development of safer, more

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economical, more rapid, and more reproducible research and diagnostic procedures (Column 2, line 59 to column 3, line 17).” An ordinary practitioner would have been motivated to combine and substitute the modified nucleotide or nucleotide analog of Ward et al. into the nucleic acid sequence amplification method of Kacian et al in view of Jones , in order to achieve the express advantages, as noted by Ward et al, of a method which permit the development of safer, more economical, more rapid, and more reproducible research and diagnostic procedures.

10. Claims 1-6 and 8-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kacian et al. (U.S. Patent 5,399,491) (March 21, 1995) in view of Jones (U.S. Patent 6,190,889 B1) (February 20, 2001) further in view of Ward et al. (U.S. Patent 4,711,955) (December 8, 1987) further in view of Dahlberg et al. (U.S. Patent 5,871,911) (February 16, 1999).

Kacian et al. in view of Jones further in view of Ward et al. teach the method of claims 1-46 as described above.

Kacian et al. in view of Jones further in view of Ward et al do not teach one or more specific unmodified primers comprising at least one non-complimentary sequence to a distinct sequence of the specific nucleic acid, such that upon hybridization to the specific nucleic acid at least one loop structure is formed.

Dahlberg et al teach one or more specific unmodified primers comprising at least one non-complimentary sequence to a distinct sequence of the specific nucleic acid, such that upon hybridization to the specific nucleic acid at least one loop structure is formed. (Figure 3, Column 6, line 60 to Column 7, line 5).

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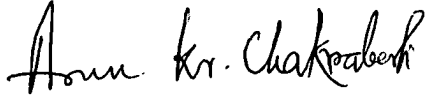
It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the primer having loop structure of Dahlberg et al. into the method of Kacian et al. in view of Ward et al ., since Dahlberg et al. state, "In this case, the pilot oligonucleotide has a 3' terminal hairpin that acts as an integral primer. The looped end of the hairpin may be of a specific sequence called a tetra-loop, which confers extraordinary thermostability on the stem-loop structure (Column 6, lines 61-65)." An ordinary practitioner would have been motivated to combine and substitute the primer having loop structure of Dahlberg et al. into the method of Kacian et al. in view of Ward et al . in order to achieve the express advantages , as noted by Dahlberg et al., of a looped end primer which confers extraordinary thermostability on the stem-loop structure.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W.Gary Jones, can be reached on (703) 308-1152. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located In Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or

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(703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published In the Official Gazette, 1096 OG 30 (November 15, 1989).



Arun Chakrabarti

Patent Examiner

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February 22, 2001



**JEFFREY FREDMAN
PRIMARY EXAMINER**